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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,847	04/27/2006	Giovanni Cipoletti	207,567	6763

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EXAMINER	
KOSAR, AARON J	

ART UNIT	PAPER NUMBER
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,847	CIPOLETTI ET AL.	
	Examiner	Art Unit	
	AARON J. KOSAR	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/9/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of the species election in the reply filed on December 4, 2007 is acknowledged. Applicant's election species (b) of the combination of the taxonomic species of microorganism *Streptococcus thermophilus* and *Lactobacillus bulgaricus* is acknowledged.

Applicant's traversal of species (c) - that strong or weak bases or buffer function for the purpose of attenuating the pH of a more-acidic-than-desired solution and that such bases and the selection thereof for the intended purpose are universally known in the art (e.g "by every chemistry student") – *is* found to be persuasive. For the sake of compact prosecution, the species election of type of base is herein withdrawn.

Applicant has also argued that species (a), milk and milk serum, are obvious lactose-containing compositions. In view of Applicant's admission, the requirement for restricting between milk and milk serum is withdrawn.

Applicant has argued that the micro-organisms of the instant invention consume glucose, but not galactose. This is not found to be persuasive, because Applicant has argued limitations not required by the claims, i.e. the claims do not preclude a net increase in galactose with a degree of galactose consumption.

Additionally, Applicant has argued that pH control is the core/critical feature of the method; however, this is not found to be persuasive, because pH control, anticipating the claimed range and using inorganic base (NaOH) to produce net increases in galactose (neutralize lactic

acid/acidification inhibition) in ferments, are known (ACUNA, citation below), and thus cannot be the special technical/core feature.

Claims 1-20 are pending. Claim 4 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on December 4, 2007. The election/restriction requirement is still deemed proper and therefore made FINAL.

Claims 1-3 and 5-20 are pending and have been examined on the merits.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on November 9, 2006, has been considered and placed in the Application file.

Claim Objections

Claims 1, 7 and 16 are objected to because of the following informalities:

In claim 1, the word "step" in the claim preamble appears to be a typographical error of the word "steps".

In claim 7, the taxonomic genera, but not the species, are properly capitalized (e.g. *Streptococcus thermophilus, Lactobacillus bulgaricus, Lactobacillus casei*).

In claim 16, the term "concentrated at warm under vacuum" appears to be a literal translation of the foreign language document.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-18, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Claims 1-3, 5-18, and 20 are incomplete for omitting essential steps. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The minimum requirements for method steps minimally include a *providing/contacting step* in which the necessary reagents and the reaction of the sample with said reagents is recited; a *detecting/reacting step* in which the reaction steps are quantified, visualized, or effected; and a *concluding/correlating step* describing how the steps/results of the reaction allow for/provide the product .

The claims are drawn to "a process for the preparation of galactose" (method of making galactose), however, the claims positively recite the active steps of "obtaining galactose and glucose" and "maintaining a constant pH value at pH≤7.5 for a period of time ranging between 16 and 24 hours, by adding a base, strong or weak, of inorganic origin" are the only positively recited active steps in the claims. The claims are incomplete because they lack a providing/ contacting step(s) and are missing a concluding/correlating step(s).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5-18, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3, 5-18, and 20 recite the limitations "the solution..from step (i)", "the desired galactose solution..from step (ii)" There is insufficient antecedent basis for this limitation, because, step (i) does not recite the formation or presence of a solution and step (ii) does not recite a galactose solution.

Claims 16 and 17 recite the limitation "the biomass". There is insufficient antecedent basis for this limitation, because claim 1 does not recite a biomass.

Claim 20 recites the limitation "said base, strong or weak, of inorganic origin is selected from the group consisting of..sodium hydroxide, .. ammonia". There is insufficient antecedent basis for this limitation in the claim, because the species within the Markush group of bases of inorganic origin are not both strong and weak bases and thus must be associated with the appropriate subgroup (strong or weak). This ground of rejection; however, may be overcome for example by cancelling the relative terms "strong or weak" *or* by amending to separate the claimed elements to recite:

"..in which said base of inorganic origin is:

(a) a strong base selected from the group consisting of.. or

(b) a weak base selected from the group consisting of..ammonia."

Because the claims lack antecedence, it is unclear as to what elements/active steps the recited limitations are drawn and one would not be apprised as to the subject matter embraced by the claims, thus rendering the claims indefinite.

Claims 1-3, 5-18, and 20 are indefinite, because claims 1 and 18 are unclear. Claims 1 and 18 are unclear, because the preamble to claim 1 recites a method of preparing galactose from (milk) serum "not subjected to and preliminary and purification treatment.."; however, claims 1 recites the starting material species of "milk serum" and claim 18 further recites that prior to step (i) the milk/milk serum may be subjected to pasteurization, each of which recitation may broadly and reasonably be interpreted as a preliminary and purification treatment or a pretreated, purified compounds therefrom. Because the body and method step of the claims are internally inconsistent with the preamble, one would not be apprised as to the subject matter Applicant intends to embrace by the claims, rendering the claims indefinite.

Claims 1-3 and 5-20 are unclear because the term "non-modified microorganisms" is unclear. The term "non-modified" is not defined in the specification and thus one would not be apprised as to what modifications are embraced by "non-modified" or how one would distinguish (or preclude) a modified versus non-modified organism. Microorganismal genera, species, and strains may be broadly and reasonably considered modified or mutants of their hierarchal/ancestral/closely-related microorganisms and thus a degree of modification (e.g. random mutation, degrees of: thermal tolerance, enzymatic performance, drug resistance, substrate utilization, etc) is intrinsic to distinguishing all microorganisms, including among naturally-occurring microorganisms, especially in absence of evidence to the contrary or of the minimal standards by which the modified versus non-modified properties are objectively

determined. This is supported by GALZY (US 3,981,773) teaching that the mutagens used merely "increase mutation *frequency*". Thus one would not be apprised as to what microorganisms or conserved characteristics therein are embraced by the term "non-modified" rendering the claims indefinite.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the active, positively recited step describing the step of "allowing" is unclear. "Allowing" *per se* does not describe a material step further limiting of the method of claim 1 and thus one would not be apprised as to the subject matter Applicant intends to embrace by the claim, rendering the method incomplete and the claims therefrom indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 6, 8-15, and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by TORINO (Torino, M.I., "Heterofermentative pattern and exopolysaccharide production by *Lactobacillus helveticus* ATCC 15807 in response to environmental pH", Journal of Applied Microbiology. 2001, 91, 846-852).

The claims are generally drawn to a method comprising: inoculating milk/serum; obtaining galactose; maintaining a constant pH over a period of time, by adding inorganic base; and recovery of a galactose solution.

TORINO anticipates the generic invention, teaching a species of *Lactobaciillus* microorganism contacted with skim milk at a controlled pH, including pH 6.2 maintained with aqueous ammonia (ammonium hydroxide); fermented for times including 16 hours, including additional 0,8,12,16,20, 24, etc. hour increments; and HPLC/chromatographic recovery of the galactose component of the product mixture (see for example, materials and methods). Torino also teaches the effect of pH on the production rates and concentrations of acids, consumption of lactose (i.e. production of glucose and galactose) sampled during exponential growth (12 hours)(table 1).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 5-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over ACUNA (Acuna, G., et al "On-Line Estimation of Biological Variables During pH Controlled Lactic Acid Fermentations" Biotechnology and Bioengineering, 1994, 44(10), 1168-1176.) and MOORE (US 2,974,044) and TURNER (Turner, K. and Martley, F. "Galactose Fermentation and Classification of Thermophilic Lactobacilli", Applied Environmental Microbiology. 1983, 45(6), 1932-1934.).

The claims are generally drawn to a method comprising: inoculating (milk) serum; obtaining galactose; maintaining a constant pH over a period of time, by adding inorganic base; and recovery of a galactose solution.

ACUNA teaches that microorganism cultures, including *S. thermophilus* and/or a *Lactobacillus* species (e.g. *L. bulgaricus*) fermented with a milk serum composition comprising: mild whey (milk serum) and 40g/L lactose (4.0%(w/v)). Acuna teaches that the fermentation produces galactose and lactic acid as the microorganisms consume lactose (figure 1). Acuna also teaches that lactate/lactic acid are inhibitory to growth and that optimal fermentation conditions for the organisms tested were:

> *(a) S. thermophilus* (i.e. *S. salivarus* subsp. *thermophilus 404*):pH 6.5,40°C;
> *(b) L. bulgaricus* (i.e. *L. delbrueckii* subsp. *bulgaricus* 398): pH 5.8,44°C; and
> (c) Mixed culture ((a)+(b)): pH 6.5, 42°C,

wherein the culture solutions were pH-controlled by adding NaOH and temperature-controlled for 5-7 hours. Acuna also teaches recovering galactose by HPLC on a cation exchange column. (see *Materials and Methods*). Acuna still further teaches that galactose-positive strains (gal^+) and galactose-negative strains (gal^-) produce galactose in low and high levels of accumulation, respectively (abstract).

MOORE teaches that pH of a fermentation media, including media wherein acids may accumulate, may be adjusted by addition of NaOH, KOH, $Ca(OH)_2$, NH_4OH, sodium carbonate, etc… within a range of 2.1 to 8.5 (column 4).

TURNER teaches that *Lactobacilli* species which are capable of cleaving lactose into lactic acid are differentiated by their abilities to metabolize glucose and/or galactose. Turner also teaches that glucose (MRS) broth supported growth for all species of *Lactobacillus* tested, that galactose (MRS) broth containing <0.01% glucose was selective for select species of Lactobacillus, and that galactose broth containing even 0.02% glucose impurity in a galactose-enriched media is sufficient to elicit false-positive results for galactose utilization which may explain the intermixed properties among species, including for example *L. bulgaricus* and *L. helveticus* (various, *e.g.* table 1). This constitutes a teaching that galactose utilization/ fermentation (gal^+ versus gal^-) may be used as a major characteristic in assessing an organism's industrial (e.g. dairy fermentation) suitability (page 1933, ¶1).

Turner also teaches that *S. thermophilus* produces galactose from lactose, that *S. thermophilus* is commonly used in combination with gal^- strains of lactobacilli, including in the production of yoghurt (page 1933, ¶3). Turner still further teaches that *S. thermophilus* and gal^- *Lactobacilli* are incapable of fermenting free galactose or the galactose moiety of lactose (page 1932, last ¶ and portion spanning page 1933).

Acuna differs from the instantly claimed invention in that Acuna is silent with respect to the consumption of glucose and fermenting for 16 to 24 hours.

It would have been obvious to use a microorganism to consume the glucose produced by lactose breakdown into galactose and glucose, because Acuna teaches species of microorganism, including, *S. thermophilus, L. bulgaricus*, and the combination thereof, which produce galactose from lactose-containing substrate. Additionally, Turner teaches that microbes of the claimed genus, *S. thermophilus*, are known to hydrolyze lactose to galactose, are known to be combined with gal$^-$ strains of *Lactobacilli*, and that gal$^-$ *Lactobacilli* (*L. lactis and L. lactis*-like or lactic acid-insensitive *L. bulgaricus*) are known (page 1932, ¶3; page 1933, ¶3 and table 1).

One would have been motivated to use a gal$^-$ microbe because Turner teaches fermenting of gal$^-$ microbes in lactose-containing culture (skim milk) to produce a residual galactose concentration.

One would have had a reasonable expectation of success in using a gal$^-$ microbe, because Acuna teaches that galactose production is affected by lactic acid/lactate and acidity, because lactose breakdown into galactose would intrinsically produce glucose which, according to Turner, supports growth of microbes of the claimed species.

It would have been obvious to ferment for 16 to 24 hours because Acuna teaches fermenting of cultures over time, including the increase of galactose in mixed culture from 0-400 minutes partially hydrolyzes the lactose present, and because Turner teaches that fermenting for 24 hours at 37°C.

One would have been motivated to optimize the time of reaction because Acuna teaches that the reaction is incomplete at the maximum time (upward sloped-trend, figure 1) and because Turner teaches reacting by fermenting for 24 hours. Additionally, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g. reaction time, temperature of an enzymatic reaction, substrate concentrations), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP § 2145.05).

Acuna, Turner, and Moore are relied upon for the reasons discussed above. If not expressly taught by these references, based upon the overall beneficial teaching provided with respect to recovery of galactose in the manner disclosed therein, the selection of a known purification method and the adjustments of particular conventional working conditions (e.g., determining one or more suitable ranges in which to perform such a puficitiaon/isolation), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan, especially in the absence of evidence to the criiticallity of a particular feature in effecting galactose production and recovery as claimed or in the absence of evidence to the contrary.

The MPEP states, “A prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. “An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the

art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and *In re Dillon*, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991)." *See* MPEP § 2144.09. In the instant case it would have been obvious to substitute NaOH for another base, because MOORE teaches that NaOH, KOH, $Ca(OH)_2$, $NH_4(OH)$, etc. are known inorganic bases, having known metal-hydroxide/metal-carbonate chemical structures, and functioning for the same utility, to effect pH control of fermentation media.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 1-3 and 5-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over GALZY (US 3,981,773 (PTO-1449, 11/9/2006)) in view of ACUNA (Acuna, G., et al. Biotechnology and Bioengineering, 1994, 44(10), 1168-1176.) and MOORE (US 2,974,044) and TURNER (Turner, K. and Martley, F. Applied Environmental Microbiology. 1983, 45(6), 1932-1934.).

The claims are drawn as described above.

The teachings of TURNER, and MOORE, and ACUNA are as presented above. Turner and Acuna generally teach combinations of bacteria useful in producing galactose from lactose-containing substrates and the conditions affecting galactose production, including pH by addition of NaOH, time of reaction, etc.. Moore generally teaches known metal hydroxide and metal carbonate species of base useful in adjusting pH.

GALZY teaches fermenting with microorganisms; converting lactose-containing compositions, including milk serum; fermenting for a period of time, including 48 or 72 hours or, for bacteria, the "fermentation process is more rapid"(column 3); and optionally recovering galactose; however, the instant claims differ from GALZY in that Galzy is silent with respect to controlling pH.

GALZY teaches "treatment of solutions containing lactose, in particular lactoserum, or milk with microorganisms to produce,..a solution of galactose"(column 1, Summary, ¶1). Galzy also teaches that microorganisms (i.e. yeast) which assimilate glucose, but not galactose are known (column 1). Galzy further teaches preferred embodiments using selection from strains exposed to mutagens and selection of strains (i.e. directed evolution to select the most favorable strain(s)). Galzy additionally teaches the desirability of selecting a microorganism have β-

galactosidase (milk/lactoserum/lactose digesting ability) and which is galactose-utilization/fermentation negative (gal$^-$). Galzy also teaches optionally extracting/recovering galactose from the galactose solution (column 1, Summary, ¶1; column 3, last ¶ and portion spanning column 4; examples). Galzy further teaches that lactose-containing solutions may be provided from a variety of sources "not limited to lactoserums" (column 1, last ¶; claims 13, 14).

GALZY teaches beneficially using lactoserum substrate and microorganisms which have β-galactosidase (EC 3.2.1.23) activity ("β-galactosidase$^+$") and are galactose fermentation-negative (gal$^-$). Galzy teaches selecting microorganisms of the taxonomic family *Lactobacteriaceae* (e.g. includes *Lactobacillus*)(column 5).

However, Galzy differs from the instant claims in that Galzy is silent regarding the elected combination of species of *Lactobacilli* and *Streptococcus*, pH control, and reaction for 16 to 24 hours.

It would have been obvious to use microorganisms including *S. thermophilus* and *L. bulgaricus* because Galzy teaches that organisms having β-galactosidase$^+$ and gal$^-$ are useful in the invention and because Turner teaches β-galactosidase activity in teaching that *S. thermophilus* produces galactose from lactose, that *S. thermophilus* is commonly used in combination with gal$^-$ strains of lactobacilli, including in the production of yoghurt (page 1933, ¶3). Turner still further teaches gal$^-$ organisms in teaching that the β-galactosidase$^+$ species, *S. thermophilus*, and *Lactobacilli* are incapable of fermenting free galactose or the terminal galactoside moiety of lactose (page 1932, last ¶ and portion spanning page 1933).

One would have been motivated to use the combination of microorganisms because Galzy teaches the selection of organisms based on β-galactosidase$^+$ and gal$^-$, and because turner

teaches that S. thermophilus and gal⁻ lactobacilli are known to be useful together and that *S. thermophilus* and select *L. bulgaricus* are each useful for the same purpose of producing galactose from lactose-containing compositions (lactose, skim milk, in yoghurt production, etc.).

One would have had a reasonable expectation of success in using the combination of microbes for the purpose of producing galactose, because each microbe is separately known to be useful for the same purpose of producing galactose from a lactose-containing substrate and thus would be obvious to combine the microbes to yield the known and predictable result.

It would have been obvious to control pH, temperature, or react for 16 to 24 hours because pH, temperature, and reaction time are known variable effecting microbial/enzymatic reactions. One would have been motivated to optimize the time of reaction because Acuna teaches that the reaction of *S. thermophilus* and *L. bulgaricus* is incomplete at the maximum time (upward sloped-trend, figure 1) and because Turner teaches reacting by fermenting for 24 hours. Additionally, it would have been obvious to one skilled in the art at the time of invention to determine all optimum and operable conditions (e.g. reaction time, temperature of an enzymatic reaction, substrate concentrations), because such conditions are art-recognized result-effective variables that are routinely determined and optimized in the art through routine experimentation. ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). See MPEP § 2145.05).

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the

forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AARON J. KOSAR whose telephone number is (571)270-3054. The examiner can normally be reached on Monday-Thursday, 7:30AM-5:00PM, ALT. Friday,EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Aaron J Kosar/
Examiner, Art Unit 1651

/Sandra Saucier/
Primary Examiner, Art Unit 1651